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EXAMINER	
YANG, NELSON C	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,156	LINDER ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 November 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,13,15,17-19,22,28,30,31,34-37,81,82 and 93-98* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4-11,13,15,17-19,28,30,31,34,81,82,93,94 and 96-98* is/are rejected.

7)☐ Claim(s) *22,35-37 and 95* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Applicant's amendment of claims 81, 98 is acknowledged and has been entered.

2. Claims 1-2, 4-11, 13, 15, 17-19, 22, 28, 30-31, 34-27, 81-82, 93-98 are currently pending.

Rejections Withdrawn

3. Applicant's arguments, see p.7-9, filed November 11, 2010, with respect to the rejection under 35 U.S.C. 112, second paragraph have been fully considered and are persuasive. The rejection of claim 35 has been withdrawn.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 2, 6-11, 15, 17, 18, 19, 28, 94, 96 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miethe et al. [US 6,488,894] in view of Zabetakis et al. [US 5,268,147].

With respect to claims 1-2, Miethe et al. teach a reaction site comprising a reaction chamber, and multiple fluid reagents statically stored in a segregated reagent column and separated by partitions or inert and by gas bubbles or hydrophobic liquid volumes in a capillary and sealed by a closure member and a plunger (see entire publication, in publication, in particular column 2, lines 37-55, column 3, line 65 – column 4, line 10, column 6, lines 10-50,

figs 1-12). The two liquids may then be discharged in a simple, precise, chronologically defined and sequential manner into the reaction chamber without prior mixing of the reagents and wherein the reaction chamber and the reagent column may be part of a common platform (column 2, lines 30-37, fig. 1, column 35-45, claims 1-3). Miethe et al. fail to teach that the third reagent which, along with partitions, is separating the first and second liquids (see figs 1-5) and that is delivered to the reaction site is immiscible.

Zabetakis et al. teach a liquid analysis system and method that delivers a stream of successive sample liquids test packages comprising alternative segments of a sample and first reagent liquids, a buffer liquid, a second reagent liquid, and air, to a reaction site, wherein the test packages are isolated with an isolation liquid which is immiscible with the sample, buffer, and reagent liquids, and which is employed to minimize sample liquid carryover, and maximize the accuracy of the sample liquids analysis results (column 3, line 60 – column 4, line 12).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have stored the reagents in a sealed reagent column, separated by partitions or immiscible gas or liquid volumes, as suggested by Miethe et al., in order to ensure that reagents are discharged in a simple, precise, chronologically defined and sequential manner into the reaction, without requiring additional metering equipment and valves, as disclosed in Zabetakis. It would have further have been obvious to one of ordinary skill in the art at the time of the invention, to maintain the separation of the reagents of Miethe et al. by an immiscible fluid, as suggested by Zabetakis, in order to minimize any potential sample liquid carryover, and to maximize the accuracy of the sample liquids analysis results, while simplifying the reagent column by removing unnecessary elements. Furthermore, since the immiscible gas or liquid

volumes of Zabetakis et al. are inert, one of ordinary skill in the art at the time of the invention would have had a reasonable expectation of success in allowing the immiscible fluid contact the reaction site, as the inert gas or liquid volumes would not interact at the reaction sites due to their inertness.

Miethe et al. teach that the first and second fluids are maintained in a segregated reagent column, separated by a partition or a third immiscible liquid or gas, but do not teach that they are maintained for greater than one day. However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. In re Aller, 105 USPQ 233. Therefore, since the segregated reagent column is designed for statically maintaining fluids separately for storage (abstract), one of ordinary skill in the art at the time of the invention would have found it obvious to have statically maintained the fluids separately for greater than one day, for whenever the reagents are actually needed. One of ordinary skill in the art at the time of the invention would further have been motivated to maintain the reagents statically for more than a day, due to the flexibility and efficacy in being able to prepare the necessary reagents without the risk of mixing or flowing out.

6. With respect to claim 6, Miethe et al. teach a tubular receptacle (column 4, lines 35-40), which is a tube.

7. With respect to claims 7-9, Zabetakis et al. teach a pumping system at the front or back end of the system (column 2, lines 63-69, column 3, lines 3-14), which would create a pressure differential across the system (column 3, lines 3-15). Miethe et al. further disclose a specific type

of pump upstream of the reaction site comprising a plunger (column 6, lines 10-50), whereas pumping at the downstream side would involve suction.

8. With respect to claim 10, Miethe et al. do not disclose a valve, so no valves would be actuated (see entire publication).

9. With respect to claim 11, Miethe et al. do not teach actuation of any device (see entire publication).

10. With respect to claim 15, Bjornson et al. teach antibodies located in the reaction site (para. 0030).

11. With respect to claim 17, Miethe et al. teach that the separating fluid may be a gas (column 3, line 65 – column 4, line 10, column 6, lines 10-50, figs. 11-12).

12. With respect to claim 18, Zabetakis et al. teach that the sample liquid test packages may comprise buffer liquid segments to remove liquid residues and to increase the minimization of sample liquid carryover (column 18, lines 35-50). Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to for the second liquid to be a rinse solution such as a buffer in order to remove liquid residues and to increase the minimization of sample liquid carryover for additional liquid segments.

13. With respect to claims 19, 96, Zabetakis et al. teach preincubation of the sample at the reaction site prior to application of reagents (column 24, lines 10-15), which would allow for proper processing of the samples by the reagent column.

14. With respect to claim 28, Miethe et al. depict a vessel having a length to inner diameter ratio of at least 10:1 (see figs. 11-12).

15. With respect to claim 94, Miethe et al. teach a vessel with first and second branches in fluid communication (figs. 11-12).

16. Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miethe et al. [US 6,488,894] in view of Zabetakis et al. [US 5,268,147], as applied to claim 1 above, and further in view of Strand et al. [US 2002/0199094].

With respect to claims 30, 31, Miethe et al. teach the invention as discussed above and specifically teach that the reagent column comprises a capillary (column 3, line 65 – column 4, line 10), but fail to teach that the inner diameter is less than 1 millimeter or 500 microns.

Strand et al., however, teach that capillary tubes may have inner diameters that range from a few microns to about 4-5 mm, and further teach that an exemplary inner diameter for a tube is 320 μm (para. 0009). Furthermore, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. In re Aller, 105 USPQ 233.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have a capillary with an inner diameter of less than 1 mm or less than 500 microns, through normal optimization techniques known in the art, in order to obtain a desired reagent volume and flow rate.

17. Claims 4-5, 13, 93, 97, are rejected under 35 U.S.C. 103(a) as being unpatentable over Miethe et al. [US 6,488,894] in view of Zabetakis et al. [US 5,268,147], as applied to claim 1 above, and further in view of Bjornson et al. [US 2002/0092767].

With respect to claims 4, 5, 13, 93, Miethe et al. and Zabetakis et al. teach the invention as discussed above, but fail to teach that the reagent column and reaction site are integrally connected on a common platform, such as in a microfluidic device.

Bjornson et al., however, teach microfluidic chips comprising reagent reservoirs for delivering reagent plugs to reaction chambers, and further disclose that this miniaturized system of enable multiple laboratory processes to be integrated onboard a planar substrate, thus allowing for simultaneous sampling, handling, transferring, and processing of samples (para. 0021, 0031).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to integrally connected the reagent column and reaction site fo Miethe et al. in a microfluidic chip such as that disclosed by Bjornson et al., in order to allow for simultaneous sampling, handling, transferring, and processing of samples, which would allow for a larger number of assays to be performed in a shorter amount of time.

18. With respect to claim 97, Bjornson et al. teach a sample introduction port separate from the reagent reservoir (para. 0049). This would allow for application of samples, without requiring them to be included with the reagent column, thus allowing for the analysis of multiple samples to be performed.

19. Claims 34, is rejected under 35 U.S.C. 103(a) as being unpatentable over Miethe et al. [US 6,488,894] in view of Zabetakis et al. [US 5,268,147], as applied to claim 1 above, and further in view of Brock [US 2002/0001818].

With respect to claims 34, 36-37, Miethe et al. and Zabetakis et al. teach fluid segments, but fail to teach that the segments may comprise a gold-conjugated antibody or metal precursor.

Brock, however, teaches reagents comprising antibodies specific for a targeted analyte and labeled with gold, contacting the reagent with the reaction region to allow the antibody bind to the analyte, and measuring the resulting signal, which would comprise a change in light absorbance or transmission (para. 0012, 0019).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to have utilized reagents comprising antibodies specific for a targeted analyte and labeled with gold, such as those suggested by Brock, in the method of Miethe et al. and Zabetakis et al., so that labeling of specific targeted analytes during sample processing, could be performed.

20. Claims 81, 82, 98, are rejected under 35 U.S.C. 103(a) as being unpatentable over Bjornson et al. [US 2002/0092767] in view of Miethe et al. [US 6,488,894].

With respect to claims 81, Bjornson et al. teach microfluidic chips comprising reagent reservoirs for delivering reagent plugs to reaction sites which may be located within a channel (para. 0026), and further disclose that this miniaturized system of enable multiple laboratory processes to be integrated onboard a planar substrate, thus allowing for simultaneous sampling, handling, transferring, and processing of samples (para. 0021, 0031).

Miethe et al. teach a reaction site comprising a reaction chamber, and a first and second fluid reagents statically stored in a segregated reagent column and are separated by inert and substantially immiscible gas or liquid volumes (see entire publication, in publication, in particular column 2, lines 44-55, column 3, line 65 – column 4, line 10). The two liquids may then be discharged in a simple, precise, chronologically defined and sequential manner into the reaction chamber without prior mixing of the reagents and wherein the reaction chamber and the

reagent column may be part of a common platform (column 2, lines 30-37, fig. 1, column 35-45, claims 1-3).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to utilize the reagent columns of Miethe et al. as the reagent reservoirs of Bjornson et al., in order to discharge liquids in a simple, precise, chronologically defined and sequential manner onto the reaction sites of Bjornson et al., thus further increasing the speed of sample processing, while reducing the number of elements necessary to process the samples. Furthermore, since Miethe et al. is directed toward sequential dosing of reagents while avoiding mixing thereof, and since Bjornson et al. disclose that reaction sites may occur within channels, one of ordinary skill in the art at the time of the invention would have been motivated to incorporate the reaction sites into the outlet channel of Miethe et al., to ensure that reagents were delivered directly to the reaction sites without prior mixing with other reagents, thus further expediting the speed of sample processing, while also preventing any potential mixing prior to delivery of the reagents.

Miethe et al. teach that the first and second fluids are maintained in a segregated reagent column, separated by a partition or a third immiscible liquid or gas, but do not teach that they are maintained for greater than one minute. However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. In re Aller, 105 USPQ 233. Therefore, since the segregated reagent column is designed for statically maintaining fluids separately for storage (abstract), one of ordinary skill in the art at the time of the invention would have found it obvious to have statically maintained the fluids separately for greater than one minute, for whenever the reagents

are actually needed. One of ordinary skill in the art at the time of the invention would further have been motivated to maintain the reagents statically for more than a minute, due to the flexibility and efficacy in being able to prepare the necessary reagents without the risk of mixing or flowing out.

21. With respect to claim 82, Miethe et al. teach that the first and second fluids are statically maintained in the segregated reagent column, but do not teach that they are maintained for greater than one day. However, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranged involves only routine skill in the art. In re Aller, 105 USPQ 233. Therefore, since the segregated reagent column is designed for statically maintaining fluids separately for storage (abstract), one of ordinary skill in the art at the time of the invention would have found it obvious to have statically maintained the fluids separately for greater than one day, for whenever the reagents are actually needed. One of ordinary skill in the art at the time of the invention would further have been motivated to maintain the reagents statically for more than a day, due to the flexibility and efficacy in being able to prepare the necessary reagents without the risk of mixing or flowing out.

Allowable Subject Matter

22. Claims 22, 35-37, and 95 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Response to Arguments

23. Applicant's arguments filed November 11, 2010 have been fully considered but they are not persuasive.

In particular, applicant argues on p.9-11 that Miethe et al. teaches away form transferring an immiscible fluid from the vessel along with the fluid reagents, citing that Miethe et al. teaches a hydrophilic membrane designed to prevent hydrophobic fluids from being transferred to the outlet channel.

This is not found persuasive, as Miethe et al. also discloses embodiments where there is not a hydrophilic membrane that would remove hydrophobic solutions, specifically wherein the reagent column is separated by partitions, which would still be part of the common, sealed vessel. Therefore, in this embodiment, there would be no reason to incorporate a hydrophilic membrane to remove solutions. Furthermore, while the first and second solutions would be separated by partitions, there Miethe et al. also discloses a third solution in between the partitions that would be separating the first and second solutions (see figs 1-5), and since the claim does not recite that the third solution is adjacent to the first and second solutions (as recited in claims 81 and 98), this embodiment would still read on the claim as recited. While the Office acknowledges that Miethe et al. do not disclose the third fluid between the first and second fluids as being immiscible or hydrophobic in this embodiment, Zabetakis et al. provides the necessary motivation for having this third fluid be substantially immiscible with the first and second fluids, as discussed above and in the previous office action.

Furthermore, the primary goal of Miethe et al. is to ensure the sequential dosing of reagents while avoiding mixing between reagents. Zabetakis provides a means for ensuring that this goal is obtained. Not removing the hydrophobic fluid partition would not render the

invention of Miethe inoperative, nor would it undermine the purpose of the method of Miethe et al., which is to deliver reagents sequentially without mixing thereof.

24. With respect to applicant's arguments regarding 98 and 81-82 (see p.11-12), applicant argues that the claims recite avoiding contact between the first and second fluids at least until after the fluids have been applied to the reaction site, and that the first and second fluids would necessarily contact one another while in the outlet channel because the hydrophobic volume is prevented from passing across the membrane. The Office does not find this persuasive as Miethe et al. states that the reagents are sequentially dosed and mixing is avoided (column 6, lines 45-50). If the reagents were to come in contact in the outlet as applicant argues, then mixing would occur. Applicants appear to be making the assumption that the first reagent would necessarily remain in the outlet channel until the second reagent is introduced into the outlet channel, which does not appear to be the case. Furthermore, Bjornson et al. discloses that reaction steps may occur within channels, and therefore, if applicant's arguments are correct, one of ordinary skill in the art, given Miethe's desire to sequentially dose the reagents and avoid mixing thereof prior to the dosing, would have found it obvious to incorporate the reaction sites into the outlet channel of Miethe et al., as discussed above.

Conclusion

25. No claims are allowed.

26. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is (571)272-0826. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mark Shibuya can be reached on (571)272-0806. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

28. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nelson Yang/
Primary Examiner, Art Unit 1641